

WHAT IS CLAIMED IS:

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1. A mammalian host cell comprising:

- (a) a transgene under the control of regulatory sequences directing expression thereof and flanked by AAV inverse terminal repeats;
- (b) an AAV *rep* sequence and an AAV *cap* sequence under the control of regulatory sequences directing expression thereof; and
- (c) DNA required to express an adenovirus E1a gene product, an adenovirus E1b gene product, and an adenovirus E2a gene product.

2. The host cell according to claim 1, wherein said transgene regulatory sequences comprise a promoter selected from the group consisting of a native promoter of the transgene, an inducible promoter, a tissue-specific promoter and a constitutive promoter.

3. The host cell according to claim 1, wherein said DNA which expresses said E1a gene product is a nucleic acid sequence comprising adenovirus DNA encoding said E1a gene product and a first promoter directing the expression of said E1a gene product;

said DNA which expresses said E1b gene product is a nucleic acid sequence comprising adenovirus DNA encoding said E1b gene product and a second promoter directing the expression of said E1b gene product; and

said DNA which expresses said E2a gene product is a nucleic acid sequence comprising adenovirus DNA encoding said E2a gene product and a third promoter directing the expression of said E2a gene product.

4. The host cell according to claim 3, wherein said first promoter is selected from the group consisting of a native promoter of E1a, an inducible promoter and a constitutive promoter; wherein said second promoter is selected from the group consisting of a native promoter of E1b, an inducible promoter and a constitutive promoter; and wherein said third promoter is selected from the group consisting of a native promoter of E2a, an inducible promoter and a constitutive promoter.

5. The host cell according to claim 3, wherein said first promoter and said third promoter are not identical.

6. The host cell according to claim 3, wherein said first promoter and said third promoter are identical.

7. The host cell according to claim 3 wherein said first promoter and said third promoter are inducible promoters.

8. The host cell according to claim 3 wherein said first promoter or said third promoter is an inducible promoter.

9. The host cell according to claim 1, wherein
said transgene of (a) is stably integrated into the chromosomes of said host cell, present in said host cell as an episome, or transiently expressed in said host cell;

said AAV *rep* and *cap* genes of (b) are stably integrated into the chromosomes of said host cell, present in said host cell as an episome, or transiently expressed in said host cell; and

said DNA of (c) is stably integrated into the chromosomes of said host cell, present in said host cell as an episome, or transiently expressed in said host cell.

10. The host cell according to claim 1, wherein said transgene and said E2a gene product are supplied to said host cell by a hybrid adenovirus/AAV vector.

11. The host cell according to claim 1, wherein said transgene is supplied to said host cell by an rAAV.

12. The host cell according to claim 1, wherein said transgene and said DNA required to express said E1a gene product and said E1b gene product are supplied to said host cell on the same vector.

13. The host cell according to claim 1, wherein said transgene and said DNA required to express said E1a gene product, E1b gene product and E2a gene product are supplied to said host cell by a hybrid adenovirus/AAV vector, wherein in said vector, adenovirus E1a and E1b gene sequences are functionally deleted and are replaced by said transgene, and an adenovirus E3 gene sequence is functionally deleted and is replaced with said DNA required to express said E1a gene product and said E1b gene product.

14. A method for producing recombinant adeno-associated virus (rAAV) in the absence of contaminating helper virus or wild-type virus, comprising the step of culturing the host cell of claim 1.

15. The method according to claim 14, further comprising the step of purifying the rAAV from said host cell or host cell culture.

16. The method according to claim 14, wherein said DNA consists of a first nucleic acid sequence encoding a first promoter and adenovirus DNA encoding said E1a gene product, a second nucleic acid sequence encoding a second promoter and adenovirus DNA encoding said E1b gene product, and a third nucleic acid sequence encoding a third promoter and adenovirus DNA encoding said E2a product.

17. A method according to claim 16, wherein
said first promoter is selected from the group consisting of an inducible promoter, a constitutive promoter and a native promoter for E1a;
said second promoter is selected from the group consisting of an inducible promoter, a constitutive promoter and a native promoter for E1b; and
said third promoter is selected from the group consisting of an inducible promoter, a constitutive promoter and a native promoter for E2a.

18. The method according to claim 17, wherein at least one promoter of said first promoter, second promoter or third promoter is an inducible promoter, further comprising the step of adding to said host cell culture a first inducing agent to induce said inducible promoter.

19. The method according to claim 17, wherein said first and third promoters are different inducible promoters directing the expression of each respective gene product.

20. The method according to claim 19 further comprising the steps of adding to said host cell culture a first inducing agent for inducing said first inducible promoter and a second inducing agent for inducing said second inducible promoter, whereby the ratio of expressed gene products may be varied for optimizing the production of rAAV in said host cells.

21. An rAAV produced by the method of claim 14.

22. A cell lysate comprising rAAV which is substantially free of both wildtype AAV and helper adenovirus.

23. The rAAV purified from the cell lysate of claim 22.

24. An rAAV free of both wildtype AAV and helper adenovirus.